Erectile dysfunction associated with surgery for prostate and colorectal cancer

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Treatment of both prostate and colorectal cancer is associated with high rates of erectile dysfunction, but approaches to management of this common postoperative complication differ between urology and colorectal specialties.

The diagnosis and treatment of cancer can have a negative impact on patients’ bodily functions and self-image related to sexual function. Sexual intercourse and intimacy may reduce emotional distress and improve psychological response to their cancer diagnosis. This is an important aspect of maintaining relationships; diminished satisfaction may impair psychological well-being and quality of life.1,2 There were approximately 2 million people alive in the UK after a cancer diagnosis at the end of 2008; this is expected to rise by 3 per cent per year.3 This will mainly be prostate, breast and colorectal cancer. The National Cancer Survivorship Initiative was launched in 2010 to support research into improving cancer survivors’ quality of life and enabling them to return to normal functioning, in spite of the long-term consequences of cancer treatments.3

Figure 1. Laparoscopic surgery for rectal cancer (©Mark Thomas/Science Photo Library)

COLORECTAL CANCER AND ERECTILE DYSFUNCTION

Colorectal cancer is the third most common cancer in the UK, with 39,991 new cases diagnosed in 2008; two-thirds are located in the colon and one-third in the rectum (Figure 1).4 Colorectal cancer is strongly related to age, with an estimated 86 per cent of cases diagnosed in people 60 years and older.4 In the UK, there has been a rise of approximately 20 per cent in all age groups since the mid-1970s till 2006.4 Since 2006 there has been an 11 per cent rise in those aged 60–69, which may be a result of the introduction of the national bowel cancer screening programme.4 It is estimated that approximately 50 per cent will survive
SEXUAL FUNCTION

more than five years. Improvements in diagnosis, treatment and an ageing population suggest that the proportion surviving this cancer may continue to rise.

Prevalence of sexual problems after surgery
Sexual dysfunction is common following rectal surgery, with rates of up to 76 per cent in some series (Box 1). Psychological factors such as survival anxiety, fear of stoma dysfunction and altered body image may all contribute to reduced sexual desire and erectile function (EF).

One study demonstrated that 48.7 per cent of men with normal preoperative EF had moderate or severe erectile dysfunction (ED) postoperatively. Hendren et al. performed a medium-sized survey to determine the prevalence of sexual problems following surgery for rectal cancer. 19.2 per cent of their respondents (n=99) reported a degree of ED preoperatively (versus 54.3 per cent postoperatively), 68.9 per cent had abnormal International Index of Erectile Function (IIEF) scores and 44.7 and 61.1 per cent reported that their surgery and stoma worsened their sex life. In spite of these results, only 39.4 per cent (men and women) could recall a preoperative discussion of potential sexual problems; 21.2 per cent admitted using pro-erectile aids.

Postoperative ED is multifactorial, with this study highlighting the impact of body image, presence of stoma and the patient’s partner; 18.5 per cent were embarrassed or ashamed of their body or reluctant to have sex because their body was undesirable. There was a trend towards worse outcomes with more distal pelvic manipulations. These results are disconcerting, as this was a young population (median age at surgery 59) with 90.8 per cent sexually active preoperatively.

Two recent studies have highlighted this to be an ongoing problem both in the UK and Europe. A retrospective study from Germany revealed a significant increase in the proportion recording abnormal IIEF (77.2 versus 30.3 per cent; p<0.001) and IIEF domain scores after rectal surgery compared to preoperatively. In spite of these high rates of postoperative sexual dysfunction, only 12.8 per cent received follow-up with urologists.

A cross-sectional survey from the UK of colorectal patients diagnosed and treated with curative intent revealed an ED prevalence of 75.1 per cent. Significant predictors for postoperative ED were age (odds ratio [OR] 1.06) and tumour below the recto-sigmoid junction (OR 4.05). 57 per cent of the patients were in a sexual relationship, of which 77 per cent had ED. This indicates a sexually active population, a significant proportion of whom may benefit from treatment for their ED.

BOX 1. Risk factors for sexual dysfunction after rectal surgery

- Age
- Nerve damage
- Blood loss
- Anastomotic leak
- Preoperative radiotherapy
- Presence of a stoma
- Low pelvic resections

In an audit of consenting for pelvic nerve injury in colorectal surgery, only 68 per cent of men were consented; this proportion fell as patients’ age increased. Good surgical practice states that patients have a right to information about their condition and available treatments, including complications associated with treatment, to allow them to form a balanced and considered decision.

Patients often find the discussion of sexual issues difficult and some may believe that their doctors will dismiss their ED as unimportant. In a survey by Perelman et al., 33 and 38 per cent of men found speaking about their ED impossible and embarrassing to discuss with their doctors, respectively. However, reassuringly, 50 per cent believed that their doctors were the most useful source of information.

In a poll in 1999, 71 per cent of men thought their doctor would dismiss their concerns about sexual problems; 68 per cent thought their doctor would find discussions about sexual issues uncomfortable. In another study on the long-term outcomes after colorectal resection, more than a third of rectal cancer patients refused to answer questions about sexual function. This emphasises the importance for all doctors involved in the care of these patients to initiate the discussion. Although the patient may not wish to discuss any sexual dysfunction initially, the door will have been opened for later discussion.

In spite of the false belief that the elderly have no interest in sex and are not engaged in sex, a survey of men aged 75–95 years found that 59 per cent aged 70–79 years (20.9 per cent aged 90–95 years) found sex at least somewhat important and 39.6 per cent aged 70–79 years (11 per cent aged 90–95) were sexually active.

Impact of operation type

The type of operation performed has a significant impact on the likelihood of the patient experiencing postoperative ED.
A randomised controlled trial (RCT) by Jayne et al. comparing laparoscopic and open rectal and colonic cancer surgery identified that intraoperative conversion to open surgery and performance of total mesorectal excision (TME) rather than partial mesorectal excision was associated with poor postoperative function. In addition, multivariate analysis suggested that TME patients were six times more likely to experience sexual dysfunction. There was a trend for sexual function to be worse after laparoscopic resection. However, in a prospective study comparing laparoscopic and open procedures for the treatment of rectal cancer, the incidence of new-onset sexual dysfunction at three months postoperatively was 66.6 per cent. There was no significant difference between the two groups with respect to IIEF or IIEF domain scores. It has been suggested that, although use of a laparoscopic technique may improve visualisation of the deep pelvic structures, the technical demands may also predispose to inadvertent nerve injury. This will obviously depend on the surgeon’s experience and their position with respect to their learning curve.

The extent of sexual dysfunction is dependent on nerve preservation and extended lymph node dissection after mesorectal excision. The goals of TME are to balance oncological results with urogenital functional preservation. However, macroscopic visual nerve preservation and electrophysiological nerve preservation do not always match exactly. In a study by Kneist et al., where all the patients had complete visual nerve preservation, this was only confirmed electrophysiologically in 80.8 per cent. In spite of this, 26.9 per cent lost their potency.

**Adjuvant radiotherapy**

Adjuvant radiotherapy (RT) is associated with a 1.8 times greater risk of ED in men undergoing resection for rectal cancer. Song et al. compared EF in men with rectal cancer treated with preoperative RT followed by surgery and surgery alone. Erectile function was assessed using the Sexual Health Inventory for Men questionnaire at baseline and repeated at least six months later. All the men had normal IIEF-5 scores preoperatively. The IIEF-5 score fell significantly at follow-up versus baseline in both the RT + surgery (20.31 versus 11.52; p=0.012) and surgery alone (19.86 versus 14.07; p=0.031) groups. Within the RT group, there was a significantly greater fall in IIEF-5 scores as the resection became more distal. There were similar findings in a prospective study comparing laparoscopic and open procedures for the treatment of rectal cancer.

**Treatment of ED after surgery**

The only RCT to date using a phosphodiesterase 5 (PDE5) inhibitor (sildenafil) to study the treatment of ED following rectal surgery was done in 2002. This small study randomised men a median of 5.6 years following rectal surgery to either placebo or sildenafil. Men were treated for four weeks, at which point the placebo group was given sildenafil. There were no significant differences in baseline IIEF and IIEF-EF scores between the two groups. There were significant improvements in IIEF (57.4 versus 26.7; p<0.0001) and IIEF-EF (23.6 versus 10.5; p=0.0001) scores over baseline only in the treatment group. The IIEF (57.4 versus 34.5; p=0.007) and IIEF-EF (23.6 versus 10.6; p=0.005) scores were significantly higher in the treatment group after four weeks versus placebo. Side-effects tended to be higher in the treatment group but were not significantly different (50 versus 22 per cent) and no patient discontinued treatment because of side-effects.

Nishizawa et al. again highlighted the role of PDE5 inhibitors in the treatment of postoperative ED. They found an 80 per cent incidence of ED three months following surgery for rectal cancer. Sildenafil was given to 16 men who had postoperative ED who requested treatment during follow-up; sexual function improved in 69 per cent.

**Prostate Cancer and Erectile Dysfunction**

Radical prostatectomy (RP) is the treatment for localised prostate cancer in men with a life expectancy of 10 years or more. The reported incidence of ED after RP is variable but depends on the age of the patient, preoperative EF, pre-existing medical conditions, nature of surgery (nerve sparing, unilateral versus bilateral) and the experience of the surgeon. ED rates vary from 25 to 75 per cent following RP. In spite of improvements in surgical techniques, especially with nerve-sparing procedures, many patients still experience delayed or poor recovery of EF postoperatively, with an estimated 15–80 per cent developing ED in spite of nerve-sparing RP (NSRP).

**Treatment of ED after surgery**

An RCT using tadalafil for the treatment of ED after bilateral NSRP found an improvement in both normal EF scores according to IIEF (24 versus 4 per cent; p<0.001) and an increase

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**Box 2. Risk factors for failure to recover natural erections after radical prostatectomy**

- Age greater than 60 years (relative risk [RR] 1.3)
- Non-bilateral nerve-sparing radical prostatectomy (RR 1.6)
- Presence of more than two comorbidities (RR 2.1)
- Rehabilitation commencement six months or more postoperatively (RR 2.8)
- Failure of sildenafil at 12 months postoperatively (RR 4.5)
- Preoperative erectile function status

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in the proportion of patients reporting improvement in their erections (62 versus 23 per cent; \( p<0.001 \)). The IIEF-EF scores improved significantly over baseline in the treatment group (17.5 versus 12.5) but not the placebo group (13.3 versus 12.3). There was a low rate of discontinuation because of side-effects, which was not significantly different between the two groups (5.5 versus 2 per cent treatment and placebo, respectively; \( p=0.231 \)).

The authors suggested that postoperative treatment of ED may be gradual and may take up to 24 months.

Another aspect of penile rehabilitation that is often discussed is whether daily dosing or on-demand dosing is more effective or protective. Bannowsky et al. evaluated the effect of low-dose nightly sildenafil in penile rehabilitation post NSRP. In the treatment group, 47 per cent achieved erections sufficient for intercourse compared with 28 per cent in the placebo group. This increased to 86 versus 66 per cent respectively when 50–100mg of on-demand sildenafil was added. The authors suggested that nightly PDE5 inhibitors may facilitate nocturnal erections, which may have a protective effect on baseline cavernosal function.

**Preoperative risk stratification**

Accurate patient stratification is the key to patient counselling and in the selection of the most appropriate postoperative treatment strategy. A large retrospective study of men treated with bilateral NSRP proposed a novel preoperative risk stratification tool aimed at predicting recovery of EF post bilateral NSRP. Univariate and multivariate regression models tested predictors of EF recovery and created three risk groups:

- **Low risk:** age \( \leq 65 \) years; IIEF-EF \( >26 \); Charlson score (CCI) \( <1 \)
- **Intermediate risk:** age 66–69 years; IIEF-EF 11–25; CCI \( =1 \)
- **High risk:** age \( \geq 70 \) years; IIEF-EF \( \leq 10 \); CCI \( >2 \)

The proportion with recovery of EF at three years was significantly higher in those using PDE5 inhibitors (73 versus 37 per cent; \( p<0.001 \)). There was no significant difference in recovery of EF at three years between the on-demand and the daily dosing groups (79 versus 70 per cent; \( p=0.09 \)). Age at surgery, preoperative EF and CCI score were significant predictors of postoperative EF recovery (\( p<0.04 \)). The three-year EF recovery rate differed significantly between the three risk groups: 85, 58 and 39 per cent for low-, intermediate- and high-risk groups, respectively (\( p<0.001 \)). Similar rates were observed when patients were grouped according to their use of PDE5 inhibitor.

**Timing of treatment initiation**

The optimal time to initiate treatment with a PDE5 inhibitor, dose and regimen are all debatable. In an open-label study comparing nightly intraurethral alprostadil (IUA) versus sildenafil in sexually active men with normal IIEF scores prior to NSRP, mean IIEF score was 9.9 and 10.4 in the IUA and sildenafil groups, respectively, a month postoperatively, in spite of the commencement of treatment as soon as possible following surgery. There was a trend in both groups over time towards improvement in IIEF scores, global assessment question and successful sexual attempts. The IIEF scores were generally higher in the sildenafil group than in the IUA group and were still rising at 11 months postoperatively, while those in the IUA group were tending to plateau. The compliance in both groups was high, although it was higher in the sildenafil group (98 versus 79 per cent). These results indicate that EF is affected as early as one month after surgery, in spite of early treatment.

The timing of penile rehabilitation after surgery affects recovery of EF. A study by Mulhall et al. found a significant correlation between the time of starting rehabilitation and the two-year EF score after bilateral NSRP. In their study, patients were grouped into early (started before six months) versus delayed (started after six months) rehabilitation. The two-year IIEF-EF scores were significantly higher in the early group (22 versus 16; \( p<0.001 \)). In addition, the proportion with unassisted functional erections (48 versus 30 per cent; \( p<0.01 \), sildenafil-assisted functional erections (76 versus 45 per cent; \( p<0.01 \) and normal EF scores were significantly higher in the early group. The authors concluded that starting rehabilitation after 10 months from surgery was associated with long-term moderate to severe ED.

The European Association of Urology guidelines recommend the early use of pro-erectile agents, with PDE5 inhibitors being first line, and the correction of risk factors. Daily dosing may improve recovery of EF.

**CONCLUSION**

There is no doubt that ED occurs after treatment for both rectal and prostate cancer. The rates may differ between the two, with more men already having ED prior to treatment for rectal cancer as a result of age. However, there appears to be a huge discrepancy in the research and treatment of this common postoperative complication between the urology and colorectal specialties.

Research into post-rectal cancer treatment appears to focus on the incidence of ED with different types of surgery. However, research after treatment of prostate cancer appears to focus on different types of surgery, variable uses of erectileogenic agents and adjustments of lifestyle risk factors.

Although urologists and urology specialist nurses expect to discuss sexual function with their patients on a relatively frequent basis, this is not true for colorectal surgeons or stoma nurses. The increasing rates of medico-legal claims by patients in all areas would suggest that both specialties should be liaising more closely, with the colorectal team considering a similar approach to urologists in the management of this condition. Currently, although we may assume that the urology
approach may be equally efficient in rectal patients, the evidence is simply not present, and there is a need for an RCT with collaborators from both specialties.

Declaration of interests: none declared.

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